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10/019,817	05/13/2002	Jacques Edouard Germond	112843-039	9937

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EXAMINER

KERR, KATHLEEN M

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 01/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No. 10/019,817	Applicant(s) GERMOND ET AL.	
	Examiner Kathleen M Kerr	Art Unit 1652	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 15 December 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

- a) ☒ The period for reply expires 6 months from the mailing date of the final rejection.
b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
(a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
(b) ☐ they raise the issue of new matter (see Note below);
(c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
(d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____

3. ☒ Applicant's reply has overcome the following rejection(s): see attached action.
4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☐ The a) ☐ affidavit, b) ☐ exhibit, or c) ☐ request for reconsideration has been considered but does NOT place the application in condition for allowance because: _____.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: 20-24, 26-36 and 38.

Claim(s) objected to: _____.

Claim(s) rejected: 25.

Claim(s) withdrawn from consideration: _____.

8. ☐ The drawing correction filed on _____ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____.
10. ☐ Other: _____

DETAILED ACTION

Application Status

1. In response to the previous Office action, a Final rejection (mailed on September 11, 2003), Applicants filed a response and after-final amendment received on December 15, 2003. Said amendment cancelled Claim 37 and amended Claims 22, 23, 26, 29, 30, 32, and 33; said after-final amendment has been entered. Thus, Claims 20-36 and 38 are pending in the instant Office action and will be examined herein.

Priority

2. As previously noted, the instant application is granted the benefit of priority for the European application 99112471 filed on June 30, 1999 and International Application No. PCT/EP00/05834 filed on June 23, 2000.

Compliance with the Sequence Rules

3. As previously noted, this application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). A sequence listing (containing 34 sequences) in computer readable form and paper copy was filed on December 15, 2003; said listing has been entered. However, this application fails to **fully** comply with the requirements of 37 C.F.R. § 1.821 through 1.825; Applicants' attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990).

- a) Figure 1 contains disclosure of DNA sequences without benefit of SEQ ID NOs.
- b) Figure 2 contains disclosure of DNA sequences without benefit of SEQ ID NOs.
- c) Figure 3 contains disclosure of DNA and protein sequences without benefit of SEQ ID NOs.

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If the noted sequences are in the sequence listing as filed on December 15, 2003, Applicants must amend the specification to identify the sequences appropriately by SEQ ID NO (the Examiner suggests either an amendment to the Brief Description of the Drawings or filing new Drawings with SEQ ID NOs included in the drawings themselves).

Maintained or New - Objections to the Specification

4. Previous objection to the specification for being confusing with respect to the sequence listing is maintained despite the new sequence listing filed. The sequence listing, as filed on December 15, 2003, contains 34 sequences and every SEQ ID NO is mentioned in the specification and/or the claims except SEQ ID NOs: 22-34. Thus, the inclusion of SEQ ID NOs: 22-34 in the sequence listing is confusing.

Applicants argue as follows:

“The Patent Office further alleges that the specification is objected. More specifically, the Patent Office alleges that the specification is confusing with respect to the Sequence Listing since SEQ ID NO: 22 is purportedly not disclosed in the specification and/or claims. Applicants believe that this objection is improper. Indeed, the specification has been amended to include the Sequence Listing that is attached herewith and that includes SEQ ID NO: 22.”

It is precisely the inclusion of SEQ ID NO:22 in the sequence listing, but nowhere in the remainder of the specification, that leads to the noted confusion (the objection with respect to SEQ ID NOs: 23-34 can be easily remedied with an amendment to the Brief Description of the Drawings). The inclusion of a sequence in the sequence listing that is not mentioned in the specification is confusing. Why is SEQ ID NO:22 in the sequence listing at all? How does it help describe the invention? This objection is “proper” and must be addressed by Applicants by either deleting SEQ ID NO:22 from the sequence listing or by inserting into the specification a

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description of said sequence (provided this description is not new matter). Clarification is required.

Withdrawn - Claim Objections

5. Previous objection to Claim 22 for a spelling/typographical error is withdrawn by virtue of Applicants' amendment.

6. Previous objection to Claims 24, 35, and 36 for depending from a rejected claim is withdrawn by virtue of Applicants' amendment.

7. Previous objection to Claim 26 for a spelling error is withdrawn by virtue of Applicants' amendment.

8. Previous objection to Claim 29 for having improper plural species noted is withdrawn by virtue of Applicants' amendment.

Withdrawn - Claim Rejections - 35 U.S.C. § 112

9. Previous rejection of Claim 23 under 35 U.S.C. § 112, second paragraph, as being indefinite for the term "functional peptides" is withdrawn by virtue of Applicants' amendment.

10. Previous rejection of Claim 30 under 35 U.S.C. § 112, second paragraph, as being indefinite for the phrase "incorporated into a microorganism's chromosome" is withdrawn by virtue of Applicants' amendment.

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11. Previous rejection of Claim 32 under 35 U.S.C. § 112, second paragraph, as being indefinite for the term “the DNA sequence” is withdrawn by virtue of Applicants’ amendment.

12. Previous rejection of Claims 33, 34, and 37 are rejected under 35 U.S.C. § 112, second paragraph, as being incomplete for omitting essential steps, is withdrawn by virtue of Applicants’ amendment.

13. Previous rejection of Claim 37 under 35 U.S.C. § 112, second paragraph, is withdrawn by virtue of Applicants’ cancellation of said claim.

14. Previous rejection of Claim 26 under 35 U.S.C. § 112, first paragraph, written description, is withdrawn by virtue of Applicants’ amendment.

15. Previous rejection of Claim 26 under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for DNA sequences encoding SEQ ID NO:2, does not reasonably provide enablement for DNA sequences encoding functional variants of SEQ ID NO:2, the function being to bind SEQ ID NO:9, is withdrawn by virtue of Applicants’ amendment.

Maintained - Claim Rejections - 35 U.S.C. § 112

16. Previous rejection of Claim 25 under 35 U.S.C. § 112, second paragraph, as being indefinite for the “term “catabolite responsive elements” is maintained. Applicants’ arguments have been fully considered but are not deemed persuasive for the following reasons.

Applicants argue as follows:

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“Regarding claim 25, Applicants believe that this rejection is improper. Indeed, the specification provides that the promoter region may also lack any catabolite responsive elements so that no repression in the presence of a particular carbon source may be affected. See, specification, page 3, lines 20-21. Further, an example of a catabolite responsive element is provided on page 8 of the specification as even recognized by the Patent Office. Thus, Applicants believe that one skilled in the art would consider the scope and content of the subject matter as defined in claims 25 to be clear and definite in meaning.”

While the specification uses the words found in the claim, their meaning must be clear in view of the specification and the art. As noted by Applicants, page 3 of the specification cites:

“The promoter region may also lack any catabolite responsive elements, so that no repression in the presence of a particular carbon source may be effected.”

Can any carbon source be considered? Because not all carbon sources are considered “catabolites”. The meaning from this limited description in the specification is unclear as to the metes and bounds of the term.

Additionally, as previously noted, in “the specification, an example of a CRE is described on page 8, that is SEQ ID NO:8, which is *embedded within* SEQ ID NO:9, the promoter region required to be a part of the DNA sequence” (emphasis added). Thus, it “is unclear if this region must be deleted from the claimed sequence or if any and all CRE’s must be deleted.” If the former is true, then Claim 25 does not further limit the subject matter of the previous claim since a portion of the DNA of Claim 20 has been deleted. “If the latter is true, the nature of a CRE, so that it can be discerned by one of ordinary skill in the art as a part of SEQ ID NO:9, is unclear.” Thus, the metes and bounds of the term “catabolite responsive elements” are unclear, and Claim 25 is confusing. Clarification is required.

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17. Previous rejection of Claim 25 under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for DNA sequences comprising SEQ ID NO:9 in the absence of the portion that is SEQ ID NO:8 (a catabolite responsive element or CRE), does not reasonably provide enablement for DNA sequences comprising SEQ ID NO:9 in the absence of some other portion of some other CRE sequence, is maintained. Applicants' arguments have been fully considered but are not deemed persuasive for the following reasons.

Applicants argue as follows:

“With respect to claim 25, Applicants believe that this rejection is improper. Again, the specification provides specific examples of catabolite responsive elements and further provides that the promoter region may also lack any catabolite responsive elements so that no repression in the presence of a particle carbon source may be affected. Applicants believe that the specification, such as described above, provides sufficient detail such that one skilled in the art should be able to practice the claimed invention without undue experimentation.”

In correction, the Examiner notes that the specification provides *one* example (not “specific examples” as noted above) that is SEQ ID NO:8, which is a portion of SEQ ID NO:9. No detail about the structure of CRE sequences is found. As previously noted, the “instant specification presents no guidance or working examples for the identification of other CRE sequences within SEQ ID NO. No guidance of catabolites is presented as well. Numerous catabolites and portions of the sequence must be assayed to determine other CRE sequences. Such a discovery is wholly unpredictable in light of the information described in the instant specification in combination with the art. For these reasons, Claim 25 is not enabled to the full extent of its scope.”

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Summary of Pending Issues

18. The following is a summary of the issues pending in the instant application:

- a) The application does not comply with the sequence rules.
- b) The specification stands objected to for being confusing about the presence of SEQ ID NOs:22-34.
- c) Claim 25 stands rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for the term “catabolite responsive elements”.
- d) Claim 25 stands rejected under 35 U.S.C. § 112, first paragraph, scope of enablement.

Allowable Subject Matter

19. The following is reiterated from the previous Office action:

“SEQ ID NO:9 is free of the prior art; said sequence is from the lac operon of *Lactobacillus delbrueckii* subsp. *lactis*. The promoter region, SEQ ID NO:9, is different among other subspecies of *L. delbrueckii* as evidenced in the specification and the post-filing date (Germond *et al*, 2003). Although portions of SEQ ID NO:9 may be taught in the prior art in the form of IS elements from the subspecies *bulgaricus*, the full-length of SEQ ID NO:9 is not taught in the prior art and is required in all the pending claims except Claim 7. Moreover, no evidence that the IS elements previously found were located as a part of SEQ ID NO:9 in subspecies *lactis*, with or without sequence information, as presented in the instant specification.

Any DNA sequence encoding SEQ ID NO:2 is also free of the prior art; SEQ ID NO:2 is a lac repressor protein from *Lactobacillus delbrueckii* subsp. *lactis* that is a part of the lac operon.

Leong-Morgenthaler *et al.* teach a lac operon from *L. delbrueckii* subsp. *bulgaricus* wherein the DNA sequence upstream of the permease gene, that is the same location as SEQ ID NO:9 taught in the instant specification, is similar (~75% identity) to SEQ ID NO:9; however, neither SEQ ID NO:9 nor isolated portions of the lac operon from subspecies *lactis* are taught in the prior art. Moreover, no homolog to lacR, the repressor found in the operon of *L. delbrueckii* subsp. *lactis* described in the instant specification, is taught by Leong-Morgenthaler *et al.* In fact, Germond *et al.* particularly note that ONLY the subspecies *lactis* contains the lacR repressor protein in the lac operon of all the *L. delbrueckii* subspecies.”

Conclusion

20. Claims 20-24, 26-36 and 38 are allowed. Claim 25 is rejected for the reasons identified in the numbered sections of this Office action. The specification is objected to and does not fully

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comply with the sequence rules. Applicants must respond to the issues in each of the numbered sections in this Office action to be fully responsive in prosecution.


The **FINALITY** of the Office action mailed September 11, 2003 is maintained herein.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M Kerr whose telephone number is (703) 305-1229.

The examiner can normally be reached on Monday through Friday, from 9:00am to 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on (703) 308-3804. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.


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Kathleen M Kerr
Examiner
Art Unit 1652

December 29, 2003